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NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28 Oct 21 EVENTLINE has been reloaded
NEWS 29 Oct 24 BEILSTEIN adds new search fields
NEWS 30 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 32 Nov 18 DKILIT has been renamed APOLLIT
NEWS 33 Nov 25 More calculated properties added to REGISTRY
NEWS 34 Dec 02 TIBKAT will be removed from STN
NEWS 35 Dec 04 CSA files on STN

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=> s (interleukin-11 or il-11 or interleukin11 or il11)
L1 8306 (INTERLEUKIN-11 OR IL-11 OR INTERLEUKIN11 OR IL11)

=> s l1 (P) (inflamm? or mucositis)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7 (P) '
L2 1178 L1 (P) (INFLAMM? OR MUCOSITIS)

=> s l2 (p) (treat? or administ? or therap? or method?)
3 FILES SEARCHED...
4 FILES SEARCHED...
5 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L15 (P) '
L3 682 L2 (P) (TREAT? OR ADMINIST? OR THERAP? OR METHOD?)

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, EMBASE, CANCERLIT, BIOSIS, USPATFULL, BIOTECHNO'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 299 DUPLICATE REMOVE L3 (383 DUPLICATES REMOVED)

=> s l1 (p) (mucositis)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7 (P) '
L5 79 L1 (P) (MUCOSITIS)

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, EMBASE, CANCERLIT, BIOSIS, USPATFULL, BIOTECHNO'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L6 27 DUPLICATE REMOVE L5 (52 DUPLICATES REMOVED)

=> d l5 1- ibib, abs
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=> d l6 1- ibib,abs
YOU HAVE REQUESTED DATA FROM 27 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:220397 CAPLUS
DOCUMENT NUMBER: 136:252503
TITLE: Topical formulations for delivery of interleukin-11
INVENTOR(S): Warne, Nicholas W.; Bedrosian, Camille L.; Keith, James C., Jr.; Schwerschlag, Ullrich S.; Schendel, Paul F.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022156	A2	20020321	WO 2001-US28886	20010917
WO 2002022156	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001089102	A5	20020326	AU 2001-89102	20010917

PRIORITY APPLN. INFO.: US 2000-662994 A1 20000915
WO 2001-US28886 W 20010917

AB Topical formulations of interleukin-11 are disclosed for treating a variety of disorders, including inflammatory bowel diseases (e.g., Crohn's disease, ulcerative colitis, indeterminate colitis, and infectious colitis), mucositis (e.g., oral mucositis, gastrointestinal mucositis, nasal mucositis, and proctitis), necrotizing enterocolitis, inflammatory skin disorders (e.g., psoriasis, atopic dermatitis, and contact hypersensitivity), aphthous ulcers, pharyngitis, esophagitis, peptic ulcers, gingivitis, periodontitis, and ocular diseases (e.g., conjunctivitis, retinitis, and uveitis). Multiparticulate formulations of rhIL-11, in which rh

IL-11 was sprayed onto a sucrose bead and covered with a
sealant and an enteric coating were prepd. (1 mg active ingredient/100 mg
multiparticulates) and tested in the neutropenic rat model. Orally
administered rhIL-11 provides mucosal protection against
chemotherapy-induced mucosal injury and maintains gut barrier function in
exptl. animal models. Levels of circulating endotoxin were significantly
reduced in the rhIL-11 treated rats (0.4 ng/mL) compared to the control
treated rats (4.04 ng/mL) and the quant. microbiol. for P. aeruginosa in
liver and spleen tissue was significantly reduced in the rhIL-11 treated
rats compared to the control rats.

L6 ANSWER 2 OF 27 USPATFULL
ACCESSION NUMBER: 2002:109176 USPATFULL
TITLE: Human 2-19 protein homologue, z219a
INVENTOR(S): Conklin, Darrell C., Seattle, WA, United States
Blumberg, Hal, Seattle, WA, United States
PATENT ASSIGNEE(S): ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6388064	B1	20020514
APPLICATION INFO.:	US 1998-167513		19981006 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-61712P	19971006 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Eyler, Yvonne
ASSISTANT EXAMINER: Lazar-Wesley, Eliane
LEGAL REPRESENTATIVE: Johnson, Jennifer K.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 3127
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to polynucleotide and polypeptide
molecules for z219a, a novel member of the human 2-19 protein family.
The polypeptides, and polynucleotides encoding them, may be used for
detecting human chromosomal abnormalities. The present invention also
includes antibodies to the z219a polypeptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:862621 CAPLUS
TITLE: Effect of Interleukin-11 on Ameliorating Intestinal
Damage After Methotrexate Treatment of Breast Cancer
in Rats
AUTHOR(S): Gibson, Rachel J.; Keefe, Dorothy M. K.; Thompson,
Fiona M.; Clarke, Julie M.; Goland, Gary J.; Cummins,
Adrian G.
CORPORATE SOURCE: Department of Medical Oncology, The Royal Adelaide
Hospital, Adelaide
SOURCE: Digestive Diseases and Sciences (2002), 47(12),
2751-2757
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gastrointestinal mucositis after cancer chemotherapy is an
increasing problem that is essentially untreatable once established,
although it gradually remits. The aim of this study was to investigate
the time-course and effect of interleukin-11 (IL-11) on apoptosis and intestinal morphometry as
measures of mucositis. Female DA rats were implanted s.c. with
syngeneic breast cancer and treated with methotrexate (MTX). Intestinal
morphometry was used to assess villus area, crypt length, and mitotic
count per crypt. Apoptosis was assessed by TUNEL assay in the tumor and
jejunum. Tumor proliferation was assessed by mitotic count. The
time-course study showed that MTX increased apoptosis by 28-fold in the
crypts of the small intestine and by 3-fold in the tumor, and peaked at 6
h after chemotherapy. IL-11 (100 .mu.g/kg/ twice
daily s.c.) maintained intestinal wt., and reduced the severity of
mucositis, as measured by villus area, crypt length, and mitotic
count per crypt. IL-11 at higher doses (200 .mu.g and
400 .mu.g/kg/twice daily s.c.), did not further improve villus area, crypt
length, and mitotic count per crypt. IL-11 did not
affect tumor apoptosis or proliferation. We conclude that IL-
11 attenuated mucositis by maintaining intestinal wt.
and morphometry. IL-11 did not prevent apoptosis, but
rather induced compensatory crypt cell proliferation.

L6 ANSWER 4 OF 27 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 2002192086 IN-PROCESS
DOCUMENT NUMBER: 21916472 PubMed ID: 11919725
TITLE: A phase I/II double-blind, placebo-controlled study of
recombinant human interleukin-11 for

mucositis and acute GVHD prevention in allogeneic
stem cell transplantation.
AUTHOR: Antin J H; Lee S J; Neuberg D; Alyea E; Soiffer R J; Sonis
S; Ferrara J L M
CORPORATE SOURCE: Department of Adult Oncology and Biostatistical Science,
Dana-Farber Cancer Institute, Boston, MA 02115, USA.
SOURCE: BONE MARROW TRANSPLANTATION, (2002 Mar) 29 (5) 373-7.
Journal code: 8702459. ISSN: 0268-3369.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020403
Last Updated on STN: 20020403
AB Interleukin-11 (IL-11) decreases
cytokine release and increases survival in murine BMT models. In these
systems, it reduces gut permeability, partially polarizes T cells to a Th2
phenotype, down-regulates IL-12, prevents mucositis, and
accelerates recovery of oral and bowel mucosa. We conducted a randomized
double-blind pilot study of rhIL-11 administered with cyclosporine/MTX
prophylaxis after cytoxan/TBI conditioning and allogeneic stem cell
transplantation for hematologic malignancies. Patients received rhIL-11,
50 microg/kg subcutaneously daily or placebo in a 3:1 ratio. Treatment was
administered prior to the start of conditioning and continued up to 21
days. The study was designed to assess safety with stopping rules for
cardiac arrhythmias and mortality. Although projected to accrue 20
patients, only 13 patients (10 IL-11, three placebo)
were enrolled because the early stopping rule for mortality was triggered.
Of 10 evaluable patients who received IL-11, four died
by day 40 and one died on day 85. Deaths were attributable to
transplant-related toxicity. One of three placebo recipients died of
suicide, the other two are alive. Patients receiving IL-
11 had severe fluid retention and early mortality, making it
impossible to determine whether IL-11 given in this
schedule can reduce the rate of GVHD. Grade B-D acute GVHD occurred in two
of eight evaluable patients on IL-11 and one of three
patients on placebo. The primary adverse events of the study were severe
fluid retention resistant to diuresis (average weight gain 9 +/- 4%) and
multiorgan failure in five of 10 evaluable patients. The use of IL
-11 as GVHD prophylaxis in allogeneic transplantation cannot be
recommended as administered in this trial.

L6 ANSWER 5 OF 27 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2002159106 MEDLINE
DOCUMENT NUMBER: 21887199 PubMed ID: 11890354
TITLE: Oprelvekin. Genetics Institute.
AUTHOR: Sitaraman S V; Gewirtz A T
CORPORATE SOURCE: Emory University School of Medicine, Department of
Pathology and Laboratory Medicine, Atlanta, GA 30322, USA..
ssitar2@emory.edu
SOURCE: Curr Opin Investig Drugs, (2001 Oct) 2 (10) 1395-400. Ref:
34
Journal code: 100965718. ISSN: 1472-4472.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020314
Last Updated on STN: 20021031
Entered Medline: 20021030
AB Genetics Institute has developed and launched oprelvekin (rhIL-11;
Neumega), a recombinant form of human IL-11. In
November 1997, the FDA cleared oprelvekin for the prevention of severe
thrombocytopenia and the reduction of the need for platelet transfusions
following myelosuppressive chemotherapy in susceptible patients with
non-myeloid malignancies 12703021. The product was launched at the end of
1997 [312556]. By December 1999, phase III trials for Crohn's disease (CD)
were underway [363007]. Genetics Institute had commenced a 150-patient
phase II trial for mild-to-moderate CD and mucositis and the
company planned to file regulatory procedures for the indication of CD in
1999 [271210]. An oral formulation for this indication has been developed.
Oprelvekin is also undergoing phase I clinical trials for colitis
[396157], phase II clinical trials for rheumatoid arthritis [413835] and
clinical trials for psoriasis [299644]. In March 1997, Wyeth-Ayerst became
the licensee for Europe, Africa, Latin America and Asia (with the
exception of Japan). Genetics Institute holds marketing rights for North
America [239273]. In Japan, oprelvekin is being developed by Genetics
Institute and Yamanouchi; phase III trials have commenced [295049] and
were ongoing in May 2001 [411763]. In April 1996, analysts at Yamaichi
estimated launch in 2001 and maximum annual sales of over yen 10 billion
[215896]. In January 1998, Morgan Stanley Dean Witter predicted

Yamanouchi's share of sales to be yen 1 billion in 2001, rising to yen 2
billion in 2002 [315458]. Sales of oprelvekin were US $34 million for
Genetics institute in fiscal 2000 while, in July 2001, Credit Suisse First
Boston estimated that this figure will be US $30 million and US $34
million in 2001 and 2002, respectively [416883].

L6 ANSWER 6 OF 27 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002101064 EMBASE
TITLE: Mucosal barrier injury (MBI) after intensive chemotherapy.
AUTHOR: Cioch M.
CORPORATE SOURCE: Dr. M. Cioch, Klinika Hematoonkologii, Transplantacji
Szpiku, ul. Jaczewskiego 8, 20-954 Lublin, Poland.
hematol@free.med.pl
SOURCE: Onkologia Polska, (2001) 4/2 (85-89).
Refs: 33
ISSN: 1505-6732 CODEN: OPNOAS
COUNTRY: Poland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mucosal barrier injury (MBI) is reported to affect 60% to 100% of bone
marrow transplant recipients. Oral and gut mucositis may
manifest not only locally but also by severe generalised syndromes. MBI
consists of 4 phases: inflammatory, epithelial, ulcerative-bacteriological
and healing. Modern treatment consists of amifostine, glutamine, GM-CSF,
antibiotics, antifungal drugs and parenteral nutrition agents. Future
directions are the following: IgA-IgG administered orally, KGF, EGF, TGF,
IL-11, MAD-11.

L6 ANSWER 7 OF 27 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 2001641774 MEDLINE
DOCUMENT NUMBER: 21551334 PubMed ID: 11694562
TITLE: Inflammatory cytokines and mucosal injury.
AUTHOR: Williams D A
CORPORATE SOURCE: Howard Hughes Medical Institute, Indiana University School
of Medicine, Department of Pediatrics, Indianapolis, USA..
dwilliam@iupui.edu
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS,
(2001) (29) 26-30. Ref: 51
Journal code: 9011255. ISSN: 1052-6773.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020125
Entered Medline: 20020114
AB The cause of mucosal injury in inflammatory bowel disease (IBD) is not
clear but likely involves infectious agents or other toxins followed by an
abnormal immune response in genetically susceptible individuals. The
inflammatory cytokines appear to play a key role in both the
susceptibility of some individuals and the tissue damage that accompanies
IBD. The generation of transgenic and gene-targeted (knockout) animals has
provided invaluable information regarding the cytokines and cellular
immune effectors that are important in IBD. Information from these and
other preclinical animal models, such as those involving
interleukin 11, has led to human trials testing novel
therapies for IBD and other diseases in which inflammation of the gut
mucosa is an important component. Thus, expression of inflammatory
cytokines appears to be an important target for the development of novel
therapies for IBD and other diseases in which intestinal mucosal damage
occurs, such as mucositis and graft-versus-host disease.

L6 ANSWER 8 OF 27 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 2001641772 MEDLINE
DOCUMENT NUMBER: 21551332 PubMed ID: 11694560
TITLE: Protection against mucosal injury by growth factors and
cytokines.
AUTHOR: Booth D; Potten C S
CORPORATE SOURCE: Cancer Research Campaign Epithelial Biology Group, Paterson
Institute for Cancer Research, Christie Hospital,
Manchester, UK.
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS,
(2001) (29) 16-20. Ref: 20
Journal code: 9011255. ISSN: 1052-6773.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020125
Entered Medline: 20020114
AB This article provides an overview of published studies in which growth
factors and cytokines were used to modify the sensitivity of intestinal

stem cells to a dose of radiation. In these experiments, growth factors were used to manipulate the sensitivity of stem cells in the gastrointestinal tract to reduce the severity of gastrointestinal mucositis in cancer therapy patients. Transforming growth factor beta3, interleukin 11, and keratinocyte growth factor were used. All three agents, given according to appropriate protocols, can result in a threefold to fourfold increase in the number of intestinal stem cells that survive a dose of radiation therapy. This result was assessed by using the crypt microcolony assay of stem cell functional capacity. The changes in stem cell survival that were observed resulted in increased animal survival. This increased survival was taken as a surrogate for improvement in patient well-being. The severity of diarrhea, a marker of functional impairment, was concomitantly reduced.

L6 ANSWER 9 OF 27 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 2001377270 MEDLINE
DOCUMENT NUMBER: 21328732 PubMed ID: 11436115
TITLE: Mucositis associated with stem cell transplantation: current status and innovative approaches to management.
AUTHOR: Stiff P
CORPORATE SOURCE: Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA.
SOURCE: BONE MARROW TRANSPLANTATION, (2001 May) 27 Suppl 2 S3-S11. Ref: 64
Journal code: 8702459. ISSN: 0268-3369.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20011015
Entered Medline: 20011011
AB Treatment-related morbidity, and in some cases, mortality, associated with autologous and allogeneic bone marrow transplantation has decreased in the past decade largely due to the use of blood stem cells combined with hematopoietic growth factors. However, these procedures remain morbid, with several series documenting regimen-related injury to the oral mucous membranes, the worst form of toxicity from a patient perspective. The pathophysiology of transplant-related mucositis is related to two major events: direct mucosal basal cell injury leading to atrophy and ulcerations, and local infections that can become systemic, the latter of which are exacerbated by the severe neutropenia accompanying high-dose chemotherapy. Recent investigational agents designed to interfere with these two aspects of mucositis have been developed and are showing promise in early clinical trials. In particular, keratinocyte growth factor (KGF) and interleukin-11 appear active. They increase basal cell proliferation, prevent apoptosis due to the preparative regimen, and appear to ameliorate the mucositis seen with high-dose chemotherapy regimens. Oral, nonabsorbable anti-infective agents are also being tested in an attempt to prevent both local and systemic infections. Devoid of significant side-effects, KGF is now in large phase 2 trials that, if positive, will be a significant advance in promoting less morbid transplants by reducing pain and the risk of secondary infections and thus may reduce supportive care costs.

L6 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 2000:699078 CAPLUS
DOCUMENT NUMBER: 133:280574
TITLE: Methods of treating inflammatory bowel diseases by administering IL-11
INVENTOR(S): Warne, Nick W.; Bedrosian, Camille L.; Keith, James C., Jr.; Schwertschlag, Ullrich S.; Schendel, Paul F.
PATENT ASSIGNEE(S): Genetics Institute, USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,948,402.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6126933	A	20001003	US 1998-179026	19981026
US 5679339	A	19971021	US 1995-495724	19950627
WO 9701353	A1	19970116	WO 1996-US8059	19960530
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5948402	A	19990907	US 1997-892407	19970715
US 6270759	B1	20010807	US 1999-337965	19990622

PRIORITY APPLN. INFO.: US 1995-495724 A3 19950627
WO 1996-US8059 W 19960530

US 1997-892407 A2
19970715
AB Provided by the present invention are topical formulations of
Interleukin-11 and methods for treating a variety of disorders, including inflammatory bowel diseases (e.g., Crohn's disease,
ulcerative colitis, indeterminate colitis, and infectious colitis),
mucositis (e.g., oral mucositis, gastrointestinal mucositis, nasal mucositis, and proctitis), necrotizing enterocolitis, inflammatory skin disorders (e.g., psoriasis, atopic
dermatitis, and contact hypersensitivity), aphthous ulcers, pharyngitis,
esophagitis, peptic ulcers, gingivitis, periodontitis, and ocular diseases
(e.g., conjunctivitis, retinitis, and uveitis). The topical administration of IL-11 is preferable to systemic
injections, esp. in concurrent systemic administration with
chemotherapeutic or radiotherapeutic agent for cancer.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:316803 BIOSIS
DOCUMENT NUMBER: PREV200100316803
TITLE: Preliminary results of a phase I/II double-blind,
placebo-controlled study of recombinant human
interleukin-11 (rhIL-11) for
mucositis and GVHD prevention in allogeneic
transplantation.
AUTHOR(S): Antin, Joseph H. (1); Lee, Stephanie J. (1); Harkness,
Shannon (1); Alyea, Edwin (1); Soiffer, Robert J. (1);
Rimm, Ilonna J.; Ferrara, James
CORPORATE SOURCE: (1) Dana-Farber Cancer Institute, Boston, MA USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp.
786a. print.
Meeting Info.: 42nd Annual Meeting of the American Society
of Hematology San Francisco, California, USA December
01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB GVHD is a major limitation in the successful application of marrow
transplantation to hematologic diseases. It may be due in part to
conditioning-induced tissue damage, transmigration of LPS across damaged
gut mucosa, and dysregulation of inflammatory cytokines. IL-
11 decreases cytokine release and increases survival in murine BMT
models. It reduces gut permeability, polarizes T cells to Th2 phenotype,
and down-regulates IL-12. In other murine models IL-11
prevents mucositis and accelerates recovery of oral and bowel
mucosa. rhIL-11 also is used for the prevention of severe thrombocytopenia
after chemotherapy. To determine whether these effects would improve
outcome after human transplantation, we conducted a randomized
double-blind pilot study of rhIL-11 administered with standard
cyclosporine/MTX prophylaxis after cytoxan/TBI conditioning for
hematologic malignancies. Patients were randomized to rhIL-11 50mug/kg sc
qd or placebo in a 3:1 ratio. Treatment was given within 24 hr of the
start of conditioning and continued for at most 21 d. Patient age 19-58
yr, 10 matched sib and 3 unrelated donor, 7 CML, 4 MDS 1 AML, 1 NHL. 10
received rhIL-11 and 3 received placebo. The study was designed to assess
safety with stopping rules for arrhythmias and mortality within 40 d. of
the BMT. While projected to accrue 20 patients, only 13 patients were
enrolled because the early stopping rule was triggered. 1 patient was
taken off study after a single dose because of LFT changes and is
considered evaluable for safety but not efficacy. Of 10 patients receiving
rhIL-11 and evaluable for safety, 4 died by day 40 and 1 died on day 85.
Cause of death included sepsis (2), multiorgan failure (1), and alveolar
hemorrhage (2). 1/3 placebo recipients died of suicide, the other two are
alive. Grade II-IV acute GVHD occurred in 2/8 evaluable patients on
rhIL-11 and 1/3 patients on placebo. 2/4 evaluable patients on the rhIL-11
arm developed chronic GVHD. The primary adverse events of the study were
severe fluid retention resistant to diuresis and multiorgan failure in
5/10 evaluable patients. 1-year survival of patients on rhIL-11 is 44%.
Patients receiving rhIL-11 had immediate toxicity consisting of fluid
retention and early mortality, making it impossible to determine whether
rhIL-11 given in this schedule can reduce the rate of GVHD. The use of
rhIL-11 as GVHD prophylaxis in allogeneic transplantation cannot be
recommended as administered in this trial.

L6 ANSWER 12 OF 27 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 2001045168 MEDLINE
DOCUMENT NUMBER: 20359857 PubMed ID: 10899677
TITLE: Defining mechanisms of action of interleukin-

11 on the progression of radiation-induced oral
mucositis in hamsters.
AUTHOR: Sonis S T; Peterson R L; Edwards L J; Lucey C A; Wang L;
Mason L; Login G; Ymamkawa M; Moses G; Bouchard P; Hayes L
L; Bedrosian C; Dorner A J
CORPORATE SOURCE: Division of Oral Medicine, Oral and Maxillofacial Surgery
and Dentistry, Brigham and Women's Hospital, 75 Francis
Street, Boston, MA 02115, USA.
SOURCE: ORAL ONCOLOGY, (2000 Jul) 36 (4) 373-81.
Journal code: 9709118. ISSN: 1368-8375.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207
AB Oral ulcerative mucositis is a common toxicity associated with
drug and radiation therapy for cancer. It impacts on quality of life and
economic outcomes, as well as morbidity and mortality. Mucositis
is often associated with dose limitations for chemotherapy or is a cause
for dose interruption for radiation. The complexity of mucositis
as a biological process has only been recently appreciated. It has been
suggested that the condition represents a sequential interaction of oral
mucosal cells and tissues, pro-inflammatory cytokines and local factors
such as saliva and the oral microbiota. The recognition that the
pathophysiology of mucositis is a multifactorial process was
partially suggested by the observation that interleukin-
11 (IL-11), a pleotropic cytokine, favorably
altered the course of chemotherapy-induced mucositis in an
animal model. In the current study, we evaluated a series of biologic and
morphologic outcomes to determine their roles and sequence in the
development of experimental radiation-induced mucositis and to
evaluate the effects of IL-11 in attenuating them. Our
results suggest that IL-11 favorably modulates acute
radiation-induced mucositis by attenuating pro-inflammatory
cytokine expression. Data are also presented which help define the
pathobiological sequence of mucositis.

L6 ANSWER 13 OF 27 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 2000507405 MEDLINE
DOCUMENT NUMBER: 20508296 PubMed ID: 11053801
TITLE: Prevention and management of mucositis in patients with
cancer.
AUTHOR: Herrstedt J
CORPORATE SOURCE: Department of Oncology 54 B1, Copenhagen University
Hospital, DK-2730 Herlev, Denmark..
jrhe@herlevhosp.kbhamt.dk
SOURCE: INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS, (2000 Oct)
16 (2) 161-3. Ref: 14
Journal code: 9111860. ISSN: 0924-8579.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001220
AB This review summarises the large number of locally and systemically
applied preventive and therapeutic interventions of mucositis in
patients with cancer. The need for further elucidation of the
pathophysiology and for optimisation of trial methodology is emphasised.
Data from trials in animal models and preliminary data in patients
indicate that cytokines such as interleukin-1, interleukin-
11, TGF-beta 3 and keratinocyte growth factor could reduce the
incidence of mucositis. Other potentially useful agents are the
angiogenesis-inhibiting drug thalidomide, the cytoprotector amifostine and
the pineal hormone melatonin.

L6 ANSWER 14 OF 27 MEDLINE
DUPLICATE 9
ACCESSION NUMBER: 1999287113 MEDLINE
DOCUMENT NUMBER: 99287113 PubMed ID: 10360368
TITLE: The biological basis for the attenuation of
mucositis: the example of interleukin-
11.
AUTHOR: Sonis S; Edwards L; Lucey C
CORPORATE SOURCE: Division of Oral Medicine, Oral and Maxillofacial Surgery
and Dentistry, Brigham and Women's Hospital, Boston, MA
02115, USA.
SOURCE: LEUKEMIA, (1999 Jun) 13 (6) 831-4. Ref: 42
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714

Last Updated on STN: 19990714
Entered Medline: 19990629

AB Oral mucositis is common, painful, dose-limiting toxicity of drug and radiation therapy for cancer. In granulocytopenic patients, the ulcerations which accompany mucositis are frequent portals of entry for indigenous oral bacteria often leading to bacteremias or sepsis.

The complexity of mucositis as a biological process has only recently been appreciated. The condition appears to represent a sequential interaction of the oral mucosal cells and tissues, pro-inflammatory cytokines, and local environmental factors in the mouth such as microorganisms and saliva. The recognition that the pathophysiology of mucositis is a multifactorial process has presented opportunities for intervention based on biological attenuation. Interleukin-11, a pleotropic cytokine, has a range of activities which is potentially relevant to mucositis. Consequently, it has been used successfully to modify the development, severity and course of mucositis in an animal model which closely mimics the equivalent human condition.

L6 ANSWER 15 OF 27 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 2000159268 MEDLINE
DOCUMENT NUMBER: 20159268 PubMed ID: 10694945
TITLE: Prevention and treatment of chemotherapy- and radiotherapy-induced oral mucositis: a review.
AUTHOR: Plevova P
CORPORATE SOURCE: Department of Radiotherapy, University Hospital of Ostrava, Ostrava-Poruba, Czeck Republic.. pavlina.plevova@fnspo.cz
SOURCE: ORAL ONCOLOGY, (1999 Sep) 35 (5) 453-70. Ref: 225
Journal code: 9709118. ISSN: 1368-8375.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000316

AB Oral mucositis is a distressing toxic effect of systemic chemotherapy with many commonly utilized drugs and of head and neck irradiation in patients with cancer. The agents and methods that have been used and studied in chemotherapy- and radiotherapy-induced oral mucositis, their mechanisms of action, and the current knowledge of their efficiency to reduce the incidence, severity or shorten the duration of oral mucositis are reviewed in this article. Oral cooling is a cheap and available method to lower the severity of bolus 5-fluorouracil-induced oral mucositis. However, more effective methods are needed. Results of studies with granulocyte-macrophage colony-stimulating factor or granulocyte colony-stimulating factor are promising. Lasers are partly beneficial, but equipment-demanding.

Modification of the chemotherapy regimen resulting in shortening of the exposition time to chemotherapy agents or chronomodulation of chemotherapy has been shown to lower mucosal toxicity of some regimens. Results of animal studies with locally applied transforming growth factor beta 3 and interleukin-11 are also promising. Based on the findings of the role of the inflammatory cascade in the response of normal tissues to chemotherapy and radiotherapy, anti-inflammatory drugs might be beneficial. At the present time, no agent has been shown to be uniformly efficacious and can be accepted as standard therapy of chemotherapy- and radiotherapy-induced oral mucositis. Further intensive research is needed.

L6 ANSWER 16 OF 27 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 2000500979 MEDLINE
DOCUMENT NUMBER: 20499948 PubMed ID: 11045187
TITLE: [New cytokines and their role in supportive care].
Nove cytokiny a jejich mozne uplatneni v podpurne lecbe.
AUTHOR: Klener P; Trneny M
CORPORATE SOURCE: 1. interni klinika 1. lekarske fakulty a VFN Praha.
SOURCE: VNITRNI LEKARSTVI, (1999 Apr) 45 (4) 238-42. Ref: 38
Journal code: 0413602. ISSN: 0042-773X.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001109

AB Several cytokines stimulating hematopoiesis, mainly lineage restricted, are already widely used in supportive care to correct myelosuppression or anaemia (GM-CSF, G-CSF, EPO). The new growth factor are tested in

preclinical or clinical studies to abrogate other anti-cancer therapy side-effects (thrombocytopenia, mucositis etc.). IL-3 has been shown to have only limited effect on neutrophils and platelets production respectively. IL-6 and IL-11 have been tested to improve thrombocytopenia and mucositis (IL-11). Thrombopoetin (TPO, c-mpl) is tested in clinical trials and shows very strong effect on platelet counts. Stem cell factor (SCF) has shown to improve progenitor cell mobilisation, particularly in combination with other cytokines. The new promising factor, FLT-3 ligand, combines effect on hematopoiesis with effect on dendritic cells generation. The new group of synthetic cytokines (daniplestim, myelopoetin, promegapoetin and progenipoetin) is now tested in preclinical and clinical studies.

Mucositis could be influenced by new keratinocyte growth factor (KGF), which is now in phase I trials.

L6 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
ACCESSION NUMBER: 1998:583825 CAPLUS
TITLE: The therapeutic utility of Interleukin-II in the treatment of inflammatory disease
AUTHOR(S): Trepicchio, William L.; Dorner, Andrew J.
CORPORATE SOURCE: Department of Preclinical Molecular and Cellular Biology, Genetics Institute, Andover, MA, 01810, USA
SOURCE: Expert Opin. Invest. Drugs (1998), 7(9), 1501-1504
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin-11 (IL-11) is a pleiotropic cytokine that exhibits anti-inflammatory and mucosal protective effects in a variety of animal models of acute and chronic inflammation, such as mucositis, inflammatory bowel disease and autoimmune joint disease. This redn. in inflammation and epithelial damage is mediated in part through effects of recombinant human (rh) IL-11 on macrophage effector function and epithelial cell growth. In vitro studies indicate that rhIL-11 inhibits tumor necrosis factor (TNF)-.alpha., IL-1.beta., IL-12, IL-6, and nitric oxide prodn. from activated macrophages. Anal. of the effects of rhIL-11 on transcription factors that activate pro-inflammatory cytokines demonstrate that the level of induced nuclear factor kappa B (NF-.kappa.B) binding activity in the nucleus of rhIL-11-treated peritoneal macrophages is significantly reduced. Studies of normal intestinal epithelial cells indicate that rhIL-11 reduces the rate of cellular proliferation. Anal. of cell-cycle progression demonstrates that growth inhibition of epithelial cells by rhIL-11 correlates with delayed entry into S phase and suppression of pRB phosphorylation. IL-11 also protects intestinal crypt stem cells from radiation- or chemotherapy-induced insults. Such immunomodulatory and epithelial activities may contribute to the protective effects of this cytokine and support the clin. utility of rhIL-11 in the treatment of mucositis , as well as a variety of chronic inflammatory diseases, such as Crohn's disease and rheumatoid arthritis.

L6 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:406367 CAPLUS
DOCUMENT NUMBER: 129:80275
TITLE: Acceleration of recovery of small intestinal mucosal cells by IL-11
AUTHOR(S): Teramura, Masanao
CORPORATE SOURCE: Dep. Hematol., Tokyo Women's Med. Coll., Tokyo, 162, Japan
SOURCE: Ensho to Men'eki (1998), 6(4), 441-445
CODEN: ENMEFA; ISSN: 0918-8371
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 12 refs. discussing the effects of IL-11 on the recovery of small intestinal mucosal cells that have been damaged by chemotherapy, radiation, short bowel syndrome, colitis, burning, and chemotherapy-induced mucositis.

L6 ANSWER 19 OF 27 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 97392673 MEDLINE
DOCUMENT NUMBER: 97392673 PubMed ID: 9245489
TITLE: Mitigating effects of interleukin 11 on consecutive courses of 5-fluorouracil-induced ulcerative mucositis in hamsters.
AUTHOR: Sonis S T; Van Vugt A G; McDonald J; Dotoli E; Schwertschlag U; Szklut P; Keith J
CORPORATE SOURCE: Division of Oral Medicine Oral and Maxillofacial Surgery, and Dentistry, Brigham & Women's Hospital, Boston, MA 02115, USA.
SOURCE: CYTOKINE, (1997 Aug) 9 (8) 605-12.
Journal code: 9005353. ISSN: 1043-4666.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971024

Last Updated on STN: 19971024
Entered Medline: 19971014

AB Ulcerative mucositis is a painful, debilitating and dose-limiting toxicity of cancer chemotherapy. Current treatment is largely palliative and no adequate preventive treatment exists. Recently, we reported that recombinant human(rh) interleukin 11 (IL-11) favourably modified the course of mucositis following a single stomatotoxic regimen of 5-fluorouracil in hamsters. Although potentially beneficial, the clinically relevant issue of mucositis and myelosuppression during multicourse chemotherapy treatment was not addressed. The present study was undertaken to evaluate the effect of rhIL-11 on two consecutive courses of mucositis and myelosuppression in hamsters.

Ulcerative mucositis was induced using a standardized protocol consisting of 5-fluorouracil (60 mg/kg) on days 1 and 2 followed by superficial irritation of the buccal mucosa on day 4. Animals treated with 100 microg of rhIL-11 for 12 consecutive days following each regimen of chemotherapy experienced a reduction in the incidence, severity, and duration of mucositis, a reduction in weight loss, and less morbidity and mortality relative to control animals. Bone marrow cellularity and function was not adversely affected by rhIL-11 treatment.

The present study is consistent with the potential use of rhIL-11 treating patients at risk of developing ulcerative mucositis while undergoing intensive multicourse chemotherapy treatment.

L6 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14
ACCESSION NUMBER: 1998:371037 CAPLUS
DOCUMENT NUMBER: 129:134807
TITLE: Interleukin-11: biological activity and clinical studies
AUTHOR(S): Dorner, Andrew J.; Goldman, Samuel J.; Keith, James C., Jr.
CORPORATE SOURCE: Department of Preclinical Research and Development, Genetics Institute Inc., Cambridge, MA, USA
SOURCE: BioDrugs (1997), 8(6), 418-429
CODEN: BIDRF4; ISSN: 1173-8804
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 64 refs. Interleukin-11 (IL-11) is a cytokine which interacts with a variety of hemopoietic and non-hemopoietic cell types. Recombinant human IL-11 (rhIL-11; oprelvekin) is produced in E. coli and differs from the naturally occurring protein only in the absence of the N-terminal proline residue. In synergy with other factors, rhIL-11 stimulates the growth of myeloid, erythroid, and megakaryocyte progenitors in vitro. In vivo, rhIL-11 is active in mice, rats, dogs, guinea pigs, hamsters, and non-human primates, where the principal activity measured was stimulation of megakaryocytopoiesis and thrombopoiesis. RhIL-11 has shown benefit in 2 clin. trials by reducing severe chemotherapy-induced thrombocytopenia.

In addn. to its thrombopoietic activity, rhIL-11 has also shown activity in models of acute gastrointestinal mucosal damage. RhIL-11 enhanced survival in mice following cytoablative therapy and in a hamster model of chemotherapy-induced oral mucositis, where treatment with rhIL-11 was assocd. with decreased mucosal damage, accelerated healing, and reduced nos. of deaths. RhIL-11 is currently in clin. trials for the treatment of chemotherapy-induced mucositis. In rat models of acute colonic injury and inflammatory bowel disease, rhIL-11 treatment reduced intestinal mucosal damage and alleviated clin. signs. RhIL-11 has direct effects on activated macrophages to reduce the prodn. of pro-inflammatory mediators. In animal models of endotoxemia, rhIL-11 treatment reduced serum levels of pro-inflammatory cytokines and blocked hypotension. RhIL-11 increased survival in models of Gram-neg. sepsis and toxic shock. Mechanistically, rhIL-11 functions at many levels to control inflammation, ameliorate tissue damage, and maintain hemostasis in the face of trauma or infection. RhIL-11 has direct effects on hepatocytes, inducing the prodn. of acute phase reactant proteins, heme oxygenase, and TIMP-1. RhIL-11 administration has been assocd. with increased plasma levels of von Willebrand factor and fibrinogen. RhIL-11 treatment potentially offers multiple benefits for cancer chemotherapy, such as prevention of thrombocytopenia, gastrointestinal epithelial protection, and subsequent redn. of mucositis, and amelioration of inflammatory complications.

L6 ANSWER 21 OF 27 MEDLINE
DUPLICATE 15
ACCESSION NUMBER: 2000453978 MEDLINE
DOCUMENT NUMBER: 20464824 PubMed ID: 11012229
TITLE: The clinical development of recombinant human interleukin 11 (NEUMEGA rhIL-11 growth factor).
AUTHOR: Kaye J A

CORPORATE SOURCE: Clinical Research/Hematology, Genetics Institute, Inc., Cambridge, Massachusetts 02140, USA.
SOURCE: STEM CELLS, (1996) 14 Suppl 1 256-60. Ref: 26
Journal code: 9304532. ISSN: 1066-5099.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001102
AB Completed phase I and II studies of recombinant human interleukin
11 (rhIL-11) demonstrate its potential as a treatment for
chemotherapy-induced thrombocytopenia. In a phase I study, 16 women with
breast cancer received rhIL-11 (10, 25, 50, 75 or 100 microg/kg s.c. once
daily) before and during cycles of moderately dose-intensive chemotherapy.
Platelet counts increased in all patients before chemotherapy. During
chemotherapy, the mean platelet count nadirs were 67,000 cells/microl
(rhIL-11 10 microg/kg) and greater than 150,000 cells/microl (25, 50 and
75 microg/kg). Thus, doses of 25 microg/kg and higher appeared to prevent
chemotherapy-induced thrombocytopenia in this study. In a randomized,
placebo-controlled study, rhIL-11 (50 microg/kg) prevented the need for
platelet transfusions during a subsequent chemotherapy cycle in patients
who had already experienced severe chemotherapy-induced thrombocytopenia.
Among 82 evaluable patients, 8 (30%) of 27 patients administered rhIL-11
50 microg/kg avoided platelet transfusions versus one (4%) of 28 who
received placebo ($p < 0.05$). rhIL-11-treated patients received
approximately two-thirds the number of platelet transfusions that
placebo-treated patients received. The median duration of thrombocytopenia
(<50,000 cells/microl) was seven days in rhIL-11-treated patients compared
to 10 days among patients given placebo. This is the first study in which
patients with a history of severe chemotherapy-induced thrombocytopenia
who were receiving a variety of chemotherapy regimens have been shown to
avoid platelet transfusions following the administration of a
thrombopoietic growth factor. This activity of rhIL-11, and the
demonstration in preclinical models that it ameliorates
chemotherapy-induced mucositis, have promoted its further
clinical development as a supportive therapy in patients receiving
chemotherapy.

L6 ANSWER 22 OF 27 MEDLINE
DUPLICATE 16
ACCESSION NUMBER: 1998039347 MEDLINE
DOCUMENT NUMBER: 98039347 PubMed ID: 9372078
TITLE: Clinical development of recombinant human interleukin-11 to
treat chemotherapy-induced thrombocytopenia.
AUTHOR: Kaye J A
CORPORATE SOURCE: Genetics Institute, Cambridge, MA 02140, USA.
SOURCE: CURRENT OPINION IN HEMATOLOGY, (1996 May) 3 (3) 209-15.
Ref: 55
Journal code: 9430802. ISSN: 1065-6251.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971209
AB Recombinant human interleukin-11 stimulates megakaryocytopoiesis in vitro and platelet production in vivo. A clinical
program to investigate the use of recombinant human interleukin-
11 in patients with chemotherapy-induced thrombocytopenia began in
1992. These studies show the potential of recombinant human
interleukin-11 as a treatment for chemotherapy-induced
thrombocytopenia. The other activities of recombinant human
interleukin-11, such as its ability to ameliorate
mucositis in myelosuppressed animal models, may contribute to its
clinical benefits in patients receiving chemotherapy.

L6 ANSWER 23 OF 27 CANCERLIT
ACCESSION NUMBER: 96625162 CANCERLIT
DOCUMENT NUMBER: 96625162
TITLE: Interleukin-11: a new thrombopoietic agent (Meeting
abstract).
AUTHOR: Gordon M S
CORPORATE SOURCE: Indiana Univ. Medical Center, Indianapolis, IN.
SOURCE: Non-serial, (1995) 3rd International Conference: Clinical
Applications of Cytokines and Growth Factors in Hematology
and Oncology, June 8-10, 1995, Atlanta, GA, p. 31, 1995. .
DOCUMENT TYPE: (MEETING ABSTRACTS)
(CLINICAL TRIAL)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology

ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960911
Last Updated on STN: 19960911
AB Interleukin-11 is a hematopoietic growth factor in the
GP130 family of cytokines. In vitro it is synergistic with other cytokines
such as IL-3 and c-kit ligand for the proliferation of early hematopoietic
progenitors. In pre-clinical studies, IL-11 induces an
increase in the number of platelets and reduces the depth and duration of
post-chemotherapy thrombocytopenia in a variety of models. It has also
been noted that IL-11 has the ability to decrease the
development of mucositis in a murine model. IL-
11 has been well tolerated in Phase I clinical trials with side
effects comprised primarily of arthralgias and myalgias at doses greater
than 50 ug/kg. While all patients experience a therapy-related anemia, no
fevers or capillary leak syndrome was seen. Treatment with IL-
11 at doses ranging from 10-75 ug/kg results in a dose-related
increase in platelet counts. Treatment with IL-11 at
doses of 25 ug/kg and higher resulted in less thrombocytopenia as compared
to patients treated at the 10 ug/kg dose level. Phase I studies in the
setting of bone marrow transplantation have demonstrated a similar safety
profile. A recently completed randomized, placebo-controlled phase II
trial of IL-11 has demonstrated a reduction in the
incidence of platelet transfusion in patients receiving dose-intensive
chemotherapy. This improvement was especially significant for patients
receiving IL-11 at a dose of 50 ug/kg. The side effect
profile was similar to that seen in the phase I trials including anemia,
mild constitutional complaints, and symptoms related to fluid retention.
IL-11 is a new thrombopoietic agent with the potential
to impact upon chemotherapy-induced thrombocytopenia.

L6 ANSWER 24 OF 27 CANCERLIT
ACCESSION NUMBER: 95609965 CANCERLIT
DOCUMENT NUMBER: 95609965
TITLE: Effect of topical and subcutaneous administration of
interleukin-11 on chemotherapy-induced ulcerative mucositis in hamsters (Meeting abstract).
AUTHOR: Sonis S T; Dotoli E A; Muska A D; Van Vugt A G; Keith J C
CORPORATE SOURCE: Harvard School of Dental Medicine, Boston, MA, 02115.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1995) 36 A2190.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950809
Last Updated on STN: 19950809
AB The purpose of this study was to determine the effect of topically applied
interleukin-11 (IL-11, Genetics
Institute, MA) on the course of ulcerative mucositis (UM), a
painful, debilitating and dose-limiting side effect of cancer
chemotherapy, and to evaluate the effect of varying regimens of IL
-11. 95 male golden Syrian hamsters were equally divided into 5
groups (G). G1 (control) received phosphate buffered saline and 0.5%
autologous hamster serum (vehicle) topically on days (d) 3-14. G2 and 4
were given 50 ug of IL-11 sc, bid, on d 0-14 and 3-14,
respectively. 100 ug of IL-11 was administered qid
topically on d 3-14 to G3, and d 0-14 to G5. To induce UM, animals
received 60 mg/kg of 5-fluorouracil on d 0 and 2. The left buccal pouch
was superficially irritated on d 4. UM was evaluated blindly starting on d
6 by scoring standardized photographs (scale 0-10, 10 most severe).
Animals were weighed daily. Blood was taken from 3 animals per group on d
6, 10, and 14. For the entire experiment, the average mean UM scores for
all groups (G2 = 3.8, G3 = 4.1, G4 = 3.3 and G5 = 4.0) was significantly
(t-test, p less than 0.05) lower than the control (5.0). In comparing mean
UM scores by day, sc administration of IL-11 was more
efficacious than topically applied IL-11 from d 6-9.
Although not significant, G4 demonstrated mean UM scores lower than G2 for
d 9-12. This finding suggests a possible advantage to administering
IL-11 after chemotherapy. G4 had significantly higher
average % weight gain compared to G1 (d 3 and 5-8), G3 (d 6-9), and G5 (d
1-8). Significant weight loss was observed in G4 compared to G2 on d 1-3,
5, 9, and 10. On d 10, significantly higher mean platelet counts (K/uL)
were demonstrated by G2, 4, and 5, achieving values of 49.0%, 105.5%, and
87.8% greater than the control. The 14-d survival rates for G1-5 were 23%,
69%, 38%, 100% and 46%. While both sc and topical administration of
IL-11 favorably modified the course of
chemotherapy-induced UM, IL-11 given sc, d 3-14, was
the most efficacious regimen.

L6 ANSWER 25 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:186374 BIOSIS
DOCUMENT NUMBER: PREV199598200674
TITLE: Effect of topical and subcutaneous administration of
interleukin-11 on chemotherapy-induced ulcerative mucositis in hamsters.

AUTHOR(S): Sonis, S. T. (1); Dotoli, E. A.; Muska, A. D.; Van Vugt, A.
G.; Keith, J. C.
CORPORATE SOURCE: (1) Harvard Sch. Dent. Med., Boston, MA 02115 USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (1995) Vol. 36, No. 0, pp. 368.
Meeting Info.: Eighty-sixth Annual Meeting of the American
Association for Cancer Research Toronto, Ontario, Canada
March 18-22, 1995
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 26 OF 27 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 96103636 MEDLINE
DOCUMENT NUMBER: 96103636 PubMed ID: 7492924
TITLE: Alteration in the frequency, severity and duration of
chemotherapy-induced mucositis in hamsters by
interleukin-11.
AUTHOR: Sonis S; Muska A; O'Brien J; Van Vugt A; Langer-Safer P;
Keith J
CORPORATE SOURCE: Division of Oral Medicine and Dentistry, Brigham and
Women's Hospital, Boston, Massachusetts, USA.
SOURCE: EUROPEAN JOURNAL OF CANCER. PART B, ORAL ONCOLOGY, (1995
Jul) 31B (4) 261-6.
Journal code: 9214373. ISSN: 0964-1955.
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FILE SEGMENT: Dental Journals; Priority Journals
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AB Ninety-five young, male Golden Syrian hamsters were randomly divided into
five equally sized groups. One group served as a placebo control while the
animals in the others received one of four doses of interleukin-eleven (
IL-11) twice daily given by subcutaneous injection
beginning on the first day of chemotherapy (day 0) and continuing to day
14. Mucositis was induced with 5-fluorouracil using a standard
regimen of 60 mg/kg, intraperitoneally on days 0 and 2 followed by
superficial mucosal irritation on day 4. Animals were evaluated daily
beginning on day 6. Mucositis was assessed using a standardised
technique in which randomly numbered daily mucosal photographs were scored
by three blinded independent observers at the conclusion of the
experiment. IL-11 favourably affected the frequency, severity and duration of mucositis. This phenomenon appeared to
be dose dependent. Hamsters receiving 30 and 100 micrograms per day of
IL-11 demonstrated significantly ($P < 0.05$) lower
mucositis scores than did either the control or animals receiving
3 or 10 micrograms per day, although the latter had marginal beneficial
effects. Additionally, survival was significantly better for hamsters
receiving higher doses of IL-11 (85%) compared to the
placebo control (46%). IL-11 administration also
favourably affected weight loss. While stimulation of platelet production
was noted in animals receiving IL-11, a lack of
difference in bone marrow cellularity between test and control animals
suggests that the mechanism by which IL-11 modifies
mucositis is mediated at the epithelial or connective tissue level
rather than through the marrow. The kinetics of IL-11
alteration of mucositis induction supports such a hypothesis.
Further investigation is currently underway to establish a definitive
mechanism by which IL-11 protects the oral mucosa.

L6 ANSWER 27 OF 27 MEDLINE
DUPLICATE 18
ACCESSION NUMBER: 95211031 MEDLINE
DOCUMENT NUMBER: 95211031 PubMed ID: 7696971
TITLE: IL-11, a pleiotropic cytokine: exciting new effects of
IL-11 on gastrointestinal mucosal biology.
AUTHOR: Keith J C Jr; Albert L; Sonis S T; Pfeiffer C J; Schaub R G
CORPORATE SOURCE: Genetics Institute, Inc., Cambridge, Massachusetts.
SOURCE: STEM CELLS, (1994) 12 Suppl 1 79-89; discussion 89-90.
Journal code: 9304532. ISSN: 1066-5099.
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AB Recombinant human interleukin 11 (rhIL-11) is a
pleiotropic cytokine that stimulates bone marrow stem cells to proliferate
and decreases intestinal mucosal injury produced by cytoablative drugs and
radiation in animals. The effects of rhIL-11 were studied in a hamster
model of oral mucositis and in two rat models of inflammatory
bowel disease (IBD). Oral mucositis was induced in male Golden
Syrian hamsters with 5-fluorouracil 60 mg/kg intraperitoneal, days 0 and
2. Peak mucositis occurred by day 10 in vehicle treated animals.

rhIL-11, given twice daily subcutaneously, decreased the mucositis
in a dose-dependent manner and increased animal survival at all doses
tested. In two models of IBD, the acetic acid-induced acute colonic injury
model in Sprague-Dawley rats and the transgenic Fischer 344 rats
expressing human HLA-B27 and beta 2-microglobulin, rhIL-11 decreased the
gross and microscopic damage in the colons of these animals. These data
suggest that rhIL-11 exerts effects on the gastrointestinal mucosa which
ameliorate responses to injurious stimuli.

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